

Appl. No. 09/939,532  
Amdt. Dated June 18, 2003  
Reply to Office Action of December 18, 2002

### **REMARKS/ARGUMENTS**

Claims 1-12 remain in this application with claim 8 cancelled. New claims 10-12 were added by this amendment and consideration is respectfully requested.

#### **German Priority Document**

Applicants appreciate Examiner's note that a certified copy of the German priority document has not yet been filed.

#### **Information Disclosure Statement:**

The Examiner indicated that the information disclosure statement filed on June 25, 2002 did not include an adequate concise explanation of relevance of the foreign language references. A more detailed explanation is given below. Applicants respectfully request consideration of these references and for the Examiner to initial and return a copy of the June 25, 2002 IDS indicating consideration of the references listed on that form.

WO 99/36099 relates to sustained release compositions containing a physiologically active substance or its salt, hydroxynaphthoic acid or its salt and a biodegradable polymer or its salt; and to other drugs containing these compositions.

The German language Lottspeich et al., Boianalytik, Spektrum Publ., 1998, pages 201, 204 reference relates to purification and isolation strategies for peptides and proteins, including the use of chromatographic separations.

The German language Neumuller et al., Rompp's Chemical Lexicon, 1983, Franksche Publ., Page 1923 relates to ion exchangers and in particular ionic resins as well as the use of inorganic substances such as zeolite and synthetic substances such as Permutit, among others.

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**Claim Rejections under 35 USC § 112:**

Claims 1-5 and 9 are rejected under 35 U.S.C. § 112, ¶2 as being indefinite. The terms "free basic peptide" and "basic starting peptide" are believed to be unclear. The steps of the method claim 1 are believed to be unclear. In claims 3 and 4 the identity of the acid is believed to be unclear. In claim 9 the treatment intended is believed to be unclear. In claims 2 and 5 there are misspelled words.

Applicants corrects the misspelled words and amends claims 1-5 and 9 to clarify the claimed invention. The peptide in question is clearly identified at all occasions in the claims. Claims 1-5 and 9 as amended obviate the rejections under 35 U.S.C. § 112, ¶2, and reconsideration is respectfully requested.

**Claim Rejections under 35 USC § 102:**

Claims 1 and 5 are rejected under 35 USC § 102(b) as being anticipated by Schally et al. Examiner stated that Schally et al. teach the conversion of LHRH antagonists from a hydrogen fluoride salt to an acetic acid salt by using a "cation exchange column," referring to col. 13, lines 6-15 of Schally et al. Examiner believes that the method of claim 1 of this application reads on Schally et al. which discloses that a resin may be used to convert one acid salt of a peptide to another acid salt. However, at col. 13, line 12 Schally et al. disclose only the use of an "anion exchange resin." Nowhere does Schally et al. disclose a method for making a peptide salt having a pharmaceutically acceptable anion comprising the use of a mixed bed ion exchanger, wherein the mixed bed ion exchanger has strongly acidic cations and strong anion exchangers. Thus, claims 1 and 5 as amended are not anticipated by Schally et al.

Claims 6-9 are rejected under 35 USC § 102(b) as being anticipated by Engel et al. who teach a particular formulation of cetorelix acetate and embonate for use in suppressing tumor growth in rats. However, claims 6-7 and 9 as amended of this application are directed to a composition made by the method of claim 1 of this application, the efficacy of which composition as a pharmaceutical drug is highly sensitive to decomposition and

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purity of the peptide salt, and interactions of the peptide with adjuvants and other ingredients of the composition. The properties of this composition are therefore highly dependent on the steps of the method of claim 1. As shown in the specification and figure, the method of claim 1 produces a composition having long-lasting plasma concentrations after over 700 hours when administered in humans, a property quite different from the compositions based on cetrorelix acetate and embonate disclosed by Engel et al. Engel et al. show an effect on testosterone levels in rats that persists for only about 50-100 hours at best, then fades (See Engel et al. Figs. 2-4). Furthermore, the animal studies of Engel et al. are not predictive of Applicants' results in humans. Thus, claims 6-7 and 9 as amended of this application are not anticipated by Engel et al.

**Claim Rejections under 35 USC § 103:**

Claims 1-5 are rejected under 35 USC § 103(a) as being obvious over Coy et al. and Schally et al. in view of Engel et al. Coy et al. teach that LHRH analogs can be obtained as an acid salt and converted into another acid salt by using a cation exchanger or an anion exchanger. However, nowhere do Coy et al. or Schally et al. or Engel et al. teach a method for making a peptide salt having a pharmaceutically acceptable anion using a mixed bed ion exchanger, where the mixed bed ion exchanger has strongly acidic cations and strong anion exchangers. Furthermore, nothing in Coy et al. or Schally et al. or Engel et al. suggest that a peptide salt having a pharmaceutically acceptable anion can be prepared using a mixed bed ion exchanger having strongly acidic cations and strong anion exchangers. To establish a prima facie case for obviousness, the Examiner must show such a suggestion in the references and show evidence of a reasonable expectation of success. M.P.E.P. 2143. Claims 1-5 as amended are directed only to the novel method of making peptide salt compositions by using mixed bed ion exchangers, and are not directed to the compositions themselves. Thus, claims 1-5 as amended are not obvious under 35 USC § 103(a) over Coy et al. and Schally et al. in view of Engel et al.

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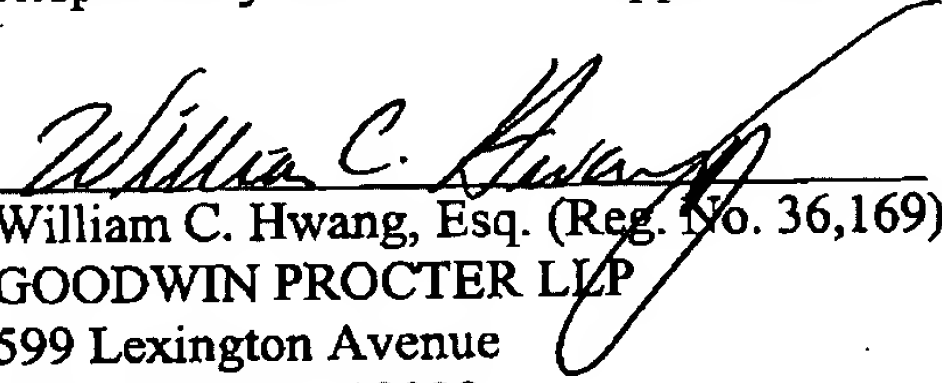
**Conclusion:**

Based on the foregoing amendments and remarks, favorable consideration and allowance of all of the claims now present in the application are respectfully requested.

Should the Examiner require or consider it advisable that the specification and/or claims be further amended or corrected in formal respects in order to place the case in condition for final allowance, then it is respectfully requested that such amendment or correction be carried out by Examiner's Amendment and the case passed to issue. Alternatively, should the Examiner feel that a personal discussion might be helpful in advancing this case to allowance, the Examiner is invited to telephone the undersigned.

The Commissioner is authorized to charge any required fees, including any extension and/or excess claim fees, any additional fees, or credit any overpayment, to Goodwin Procter LLP Deposit Account No. 06-0923.

Respectfully submitted for Applicants,

  
William C. Hwang, Esq. (Reg. No. 36,169)  
GOODWIN PROCTER LLP  
599 Lexington Avenue  
New York, NY 10022  
(212) 813-8815

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